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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,940	06/25/2007	Mitchell Ehren Garber	STAN-349	5674

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Stanford University Office of Technology Licensing
Bozicevic, Field & Francis LLP
1900 University Avenue
Suite 200
East Palo Alto, CA 94303

EXAMINER

HARRIS, ALANA M

ART UNIT	PAPER NUMBER
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1643

MAIL DATE	DELIVERY MODE
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05/21/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.		Applicant(s)	
	10/594,940		GARBER, MITCHELL EHREN	
	Examiner		Art Unit	
	Alana M. Harris, Ph.D.		1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 March 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 and 81-83 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16 and 81-83 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment and Arguments

1. Claims 1-16 and 81-83 are pending.

Claims 1, 3, 8 and 16 have been amended.

Claims 55-57 have been cancelled.

Claims 81-83 have been added.

Claims 1-16 and 81-83 are examined on the merits.

Withdrawn Objection

Specification

2. The objection of the specification is withdrawn because Applicants' have amended claims 3, 8 and 16 and attempt to incorporate subject matter into this application by reference to GenBank accession numbers Hs.516830 in claims 3, 8 and 16 is improper because this is essential subject matter. This GenBank number is considered non-patent literature that defines the limitations of the claims. This number is subject to change.

Withdrawn Rejection

Claim Rejections - 35 USC § 112

3. The rejection of claims 3, 9 and 16 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn in light of Applicants' amendments to the claims.

Maintained and New Grounds of Rejections

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. The rejection of claims 1, 2, 4-7, 9-15 and new claims 82 and 83 under 35 U.S.C. 102(b) as being anticipated by Ricci et al. (Am. J. Respir. Cell. Mol. Biol. 25: 439-446, 2001) is maintained and made.

Applicants address the standard for anticipation under 102 and note Ricci does not meet this standard, see Remarks submitted March 2, 2009, page 9. Applicants assert Ricci does not anticipate the pending claims because “[the reference] does not teach using the result of an assay for the presence of a cellular locomotion protein to evaluate metastatic potential”, see page 10 of the Remarks. Applicants’ points of view and corresponding arguments have been carefully considered, but found unpersuasive.

Applicants’ claims recite a step of “using” and newly cited wherein clause, which are not given patentable weight because it simply expresses the intended result of the process step positively recited in the “assaying” step, hence the prior

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art reads on the claims, see MPEP 2111.01 [R-3]. "Using said result..." does not appear to materially differentiate or impart any distinction from the prior art method. Moreover, using and wherein clauses do not recite any additional active method steps, but simply state a characterization or conclusion of the results of those steps.

Ricci discloses a method of assaying for the presence of neurotrophic tyrosine kinase receptor type 2 (NTRK2/TrkB), as well as other proteins associated with cellular locomotion in membranes from human bronchioloalveolar carcinoma, adenocarcinoma, squamous cell carcinoma and small cell lung cancer (SCLC) using cytoplasmic immunostaining, see Figure 2 on page 441; and page 444, bridging paragraph of columns 1 and 2, Table 2. The rejection is maintained and made for the reasons of record and set forth above.

6. The rejection of claims 1-4, 6-11, 13-16 and new claims 81-83 under 35 U.S.C. 102(b) as being anticipated by Horne et al./ U.S. Patent Application Publication number US 2002/0142981 A1 (publication date October 3, 2002) is maintained and made.

Applicants assert Horne does not teach assaying protein levels, but rather gene expression at the RNA level, see Remarks, page 11. Furthermore, "the '981 publication does not teach 'assaying said cell for the presence of at least one target protein associated with cellular locomotion to obtain a result; and using said result to evaluate said cell's metastatic propensity.", see page 11.

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Applicants' points of view and corresponding arguments have been carefully considered, but found unpersuasive.

Contrary to Applicants' assertion the publication discloses assaying protein markers for monitoring disease progression, such as the development of liver cancer, see page 8, sections 0081-0084; and page 9, sections 0088 and 0089. The relative amounts of proteins of nucleus-associated ribbon-like structure proteins, leukotriene B4 12-hydroxydehydrogenase (LTB4DH) and a cyp4 protein, cytochrome P450 were assayed, see page 9, sections 0088 and 0089; page 41, Table 6B; and page 74, Table 74.

Moreover, Horne does disclose assaying protein levels and as noted previously, Applicants' claims recite a step of "using" and newly cited wherein clause, which are not given patentable weight because it simply expresses the intended result of the process step positively recited in the "assaying" step, hence the prior art reads on the claims, see MPEP 2111.01 [R-3]. "Using said result..." does not appear to materially differentiate or impart any distinction from the prior art method. Moreover, using and wherein clauses do not recite any additional active method steps, but simply state a characterization or conclusion of the results of those steps. The rejection is maintained and made for the reasons of record and set forth above.

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7. The rejection of claims 1-4, 6-16 and new claims 82 and 83 under 35 U.S.C. 102(e) as being anticipated by Ring et al./ U.S. Patent Application Publication number US 2006/0003391 A1 (effective date August 11, 2003) is maintained and made.

Applicants argue Ring fails to disclose "...using the result of an assay for the presence of a cellular locomotion protein to evaluate metastatic potential", nor teach predictions of metastatic potential, see pages 12 and 13 of Remarks. Applicants' points of view and corresponding arguments have been carefully considered, but found unpersuasive.

The publication continue to disclose methods of classifying tumors and assaying lung tumor sample for candidate tumor biomarkers, such as cellular locomotion proteins, tripartite-containing motif 29 (TRIM29) and pregnancy-induced growth inhibitor (OKL38), which is Applicants' active step, see abstract; page 24 beginning with Example 13; page 29; and page 34.

Applicants' claims recite a step of "using" and newly cited wherein clause, which are not given patentable weight because it simply expresses the intended result of the process step positively recited in the "assaying" step, hence the prior art reads on the claims, see MPEP 2111.01 [R-3]. "Using said result..." does not appear to materially differentiate or impart any distinction from the prior art method. Moreover, using and wherein clauses do not recite any additional active method steps, but simply state a characterization or conclusion of the results of those steps. The rejection is maintained and made for the reasons of record and set forth above.

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8. The rejection of claims 1-4, 6-16 and newly added claims 82 and 83 under 35 U.S.C. 102(e) as being anticipated by Clarke/ U.S. Patent Application Publication number US 2006/0019256 A1 (effective date June 9, 2003) is maintained and made.

Applicants assert Clarke does not teach assaying protein levels and Clarke does not assay protein levels for any genes of the claimed genus, see Remarks, pages 13-15. Applicants state “the ‘256 publication does not teach ‘assaying said cell for the presence of at least one target protein associated with cellular locomotion to obtain a result; and using said result to evaluate said cell’s metastatic propensity”, see bridging pages 14 and 15. Applicants’ points of view and corresponding arguments have been carefully considered, but found unpersuasive.

Contrary to Applicants’ assertion the publication discloses assaying assaying solid tumor cancer protein markers in samples of tissue from subjects, see abstract; page 5, section 0050; page 6, sections 0061, 0065-0067; page 11, section 0113; and page 34, sections 0130 and 0131. The lung cancer types are small-cell lung, non-small cell lung cancer, adenocarcinoma of the lung, and squamous carcinoma of the lung, see page 5, section 0050. The following cellular locomotion proteins were assayed TRIM29 (page 12, line 9), LTB4DH and C20orf139 (page 19). The rejection is maintained and made for the reasons of record and set forth above.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. The rejection of claims 1-16 and newly added claims 81-83 under 35 U.S.C. 103(a) as being unpatentable over Ricci et al. (Am. J. Respir. Cell. Mol. Biol. 25: 439-446, 2001), and further in view of Horne et al./ U.S. Patent Application Publication number 2002/0142981 A1 (publication date October 3, 2002), Ring et al./ U.S. Patent Application Publication number US 2006/0003391 A1 (effective date August 11, 2003) and Clarke/ U.S. Patent Application Publication number US 2006/0019256 A1 (effective date June 9, 2003) is maintained and made.

Applicants discuss the standards for a 103 rejection, as well as the deficiencies of the references, see pages 15-17. Applicants assert the pending claim language precludes the references from reading on the claimed invention, see page 16. These arguments have been carefully considered, but found unpersuasive.

As noted in the first cited 102(b) the primary reference, Ricci still reads on Applicants' claimed invention. Ricci does not teach assaying nucleus-associated ribbon-like structure proteins, LTB4DH and a cyp4 protein, cytochrome P450.

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However, the publication '2981, now referenced as Home teaches assaying markers, LTB4DH and cytochrome P450, subfamily IVF, polypeptide 2 for monitoring disease progression, such as the development of liver cancer, see page 8, sections 0081-0084; page 41, Table 6B; and Table 7B on page 74. Publication '3391 teaches methods classifying tumors and assaying lung tumor sample for candidate tumor biomarkers, as well cellular locomotion proteins, TRIM29, OKL38, see abstract; page 24 beginning with Example 13; page 29; and page 34. Publication '19256 or Clarke teaches the following cellular locomotion proteins were assayed TRIM29 (page 12, line 9), LTB4DH and C20orf139 (page 19).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to include additional candidate biomarkers in a method of diagnosing a neoplastic disease. One of ordinary skill in the art would have been motivated to use these particular markers because the secondary references teach these markers' expression is consistent with solid cancer cell growth, see page 1, sections 0008 and 0009 of publication '2981. The rejection is maintained and made for the reasons of record and set forth above.

11. The rejection of claims 1-16 and new claims 81-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Home et al./ U.S. Patent Application Publication number 2002/0142981 A1 (publication date October 3, 2002), and further in view of Ricci et al. (Am. J. Respir. Cell. Mol. Biol. 25: 439-446, 2001),

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and further in view of Ring et al./ U.S. Patent Application Publication number US 2006/0003391 A1 (effective date August 11, 2003) and Clarke et al./ U.S. Patent Application Publication number US 2006/0019256 A1 (effective date June 9, 2003) is maintained and made.

Applicants discuss the standards for a 103 rejection, as well as the deficiencies of the references, see pages 17 and 18. Applicants assert the pending claim language precludes the references from reading on the claimed invention, see page 17. These arguments have been carefully considered, but found unpersuasive.

As noted in the first cited 102(b) the primary reference, Horne still reads on Applicants' claimed invention. Contrary to Applicants' assertion the publication discloses assaying protein markers for monitoring disease progression, such as the development of liver cancer, see page 8, sections 0081-0084; and page 9, sections 0088 and 0089. The relative amounts of proteins of nucleus-associated ribbon-like structure proteins, leukotriene B₄ 12-hydroxydehydrogenase (LTB₄DH) and a cyp4 protein, cytochrome P450, subfamily IVF, polypeptide 2 were assayed, see page 9, sections 0088 and 0089; page 41, Table 6B; and Table 7B on page 74. Horne does not teach assaying OLK38, C20orf139, TRIM29 and NTRK2/TrkB.

However, Ricci et al. (Am. J. Respir. Cell. Mol. Biol. 25: 439-446, 2001) teaches a method of assaying for the presence of NTRK2/TrkB, as well as other proteins associated with cellular locomotion in membranes from human bronchioloalveolar carcinoma, adenocarcinoma, squamous cell carcinoma and

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small cell lung cancer (SCLC) using cytoplasmic immunostaining, see Figure 2 on page 441; and page 444, bridging paragraph of columns 1 and 2, Table 2.

Ring/ Publication '3391 teaches methods classifying tumors and assaying lung tumor sample for candidate tumor biomarkers, as well cellular locomotion proteins, TRIM29, OKL38, see abstract; page 24 beginning with Example 13; page 29; and page 34. Publication '19256 or Clarke teaches the following cellular locomotion proteins were assayed TRIM29 (page 12, line 9), LTB4DH and C20orf139 (page 19). Clarke/ publication '2981, now referenced as Horne teaches assaying markers, LTB4DH and cytochrome P450, subfamily IVF, polypeptide 2 for monitoring disease progression, such as the development of liver cancer, see page 8, sections 0081-0084; page 41, Table 6B; and Table 7B on page 74.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to include additional candidate biomarkers in a method of diagnosing a neoplastic disease. One of ordinary skill in the art would have been motivated to use these particular markers because the secondary references teach these markers' expression is consistent with solid cancer cell growth, see page 1, sections 0008 and 0009 of publication '2981 or Horne. The rejection is maintained and made for the reasons of record and set forth above.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The Examiner works a flexible schedule, however she can normally be reached on 7:30 am to 6:30 pm, Monday through Saturday with alternate Fridays off.

If attempts to reach the Examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832.

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The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alana M. Harris, Ph.D.

05 May 2009

/Alana M. Harris, Ph.D./

Primary Examiner, Art Unit 1643